FILE 'CAPLUS' ENTERED AT 15:27:09 ON 07 APR 2004

=> S ASPARAGINASE;S HUMAN
          3260 ASPARAGINASE
           164 ASPARAGINASES
L1   3266 ASPARAGINASE
                (ASPARAGINASE OR ASPARAGINASES)

       1253346 HUMAN
        314839 HUMANS
L2   1413780 HUMAN
                (HUMAN OR HUMANS)

=> S L1 AND L2
L3   562 L1 AND L2

=> S L1(6A)L2
L4   170 L1(6A)L2

=> S L3 RANGE=(1950-1980)
L5   138 L1 AND L2

=> S L4 RANGE=(1950-1980)
L6   45 L1(6A)L2

=> D 1-45 CBIB ABS

L6 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1980:421652 Document No. 93:21652 Separation of L-**asparaginase** from **human** urine. Fujii, Setsuro; Takanashi, Satoyoshi; Watabe, Hidetsugu; Imamura, Yasu (Tobishi Pharmaceutical Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 55019018 19800209 Showa, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1978-90507 19780726.

AB L-Asparaginase (I) is precipitated by salting out of a human urine sample and purified by ultrafiltration, dialysis, salting out, or chromatog. The I has a mol. weight of 56,000, optimum pH at 8.0, and electrophoretic mobility (α) of 1, and was stable at pH 8.0-9.0, 50°. Thus, 3 L of fresh human urine was mixed with 300 mg bovine serum albumin and 150 mg NaN3, then with (NH4)2SO4 at 80% saturation The mixture was allowed to stand overnight at 4°, the resulting precipitate dissolved in 600 mL of a 0.1M borate buffer (pH 8.0), and centrifuged. The supernatant was concentrated with a Diaflow membrane PM-30. The concentrate was diluted with the borate buffer and again ultrafiltered. By repeating the ultrafiltration, I with an activity of 0.02 units/L urine was obtained.

L6 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1979:607148 Document No. 91:207148 **Asparaginase** production by **human** clinical isolates of Vibrio succinogenes. Radcliffe, Cynthia W.; Kafkewitz, David; Abuchowski, Abraham (Dep. Zool. Physiol., Rutgers, State Univ., Newark, NJ, 07102, USA). Applied and Environmental Microbiology, 38(4), 761-2 (English) 1979. CODEN: AEMIDF. ISSN: 0099-2240.

AB Three **human** isolates of V. succinogenes produced **asparaginase**. Apparent Kms were 87 μM, 220 μM, and 320 μM. The rate of glutamine hydrolysis was 2.8-3.5% of the rate of asparagine hydrolysis. Asparaginase production was not induced by NH4+, and enzyme yields were lower than those obtained with a rumen strain.

L6 ANSWER 3 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1979:401783 Document No. 91:1783 Separation of L-**asparaginase**-like substance from male **human** urine. Mori, Noboru; Imamura, Yasushi; Takanashi, Michiyoshi; Watabe, Hidetsugu; Sugiya, Yukio; Fujii, Setsuo (Ohmori Res. Lab., Tohbishi Pharm. Co., Ltd., Tokyo, 143, Japan). Chemical & Pharmaceutical Bulletin, 27(2), 571-2 (English) 1979. CODEN: CPBTAL. ISSN: 0009-2363.

AB L-Asparaginase activity was detected and separated from adult male human urine. Fractional salting-out with (NH4)2SO4 yielded 0.1-2.1 enzyme units of active principle/100 L. Its optimal pH is 8.0 with a stable range of pH 9.0-7.0. The elution pattern from Sephadex G-100 revealed a single enzyme peak with a mol. weight of .apprx.56,000. Urine L-asparaginase differed from that of Escherichia coli.

L6 ANSWER 4 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1979:97407 Document No. 90:97407 Mechanism of sensitivity of cultured pancreatic carcinoma to asparaginase. Wu, Ming-Chi; Arimura, Grace K.; Yunis, Adel A. (Dep. Med. Biochem., Univ. Miami Sch. Med., Miami, FL, USA). International Journal of Cancer, 22(6), 728-33 (English) 1978. CODEN: IJCNAW. ISSN: 0020-7136.

AB The effects of Escherichia coli L-**asparaginase** [9015-68-3] on cultured **human** pancreatic carcinoma (MIA PaCa-2) were studied. The enzyme (1 unit/mL) inhibited growth and protein synthesis in both MIA PaCa-2 and PANC-1, another pancreatic carcinoma cell line, but had little or no effect on human breast carcinoma or melanoma cells. The inhibition of protein synthesis by E. coli L-asparaginase was largely reversed by L-glutamine [56-85-9] but not by L-asparagine [70-47-3]. The growth of both MIA PaCa-2 and PANC-1 showed absolute dependence of L-glutamine. Apparently, the effects of E. coli L-asparaginase on cultured pancreatic carcinoma cells is exerted at least in part through its L-glutaminase activity. Although the addition of L-glutamine to the culture appeared to prevent cell death caused by L-asparaginase, it did not restore the ability of the cells to proliferate. Asparaginase derived from vibrio succinogenes, which is virtually free of L-glutaminase activity, was equally inhibitory to MIA PaCa-2 cell growth but did not affect protein synthesis. Apparently, the inhibition of growth of cultured pancreatic carcinoma cells by E. coli asparaginase is a combined function of both its L-asparaginase and L-glutaminase activity.

L6 ANSWER 5 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1978:438322 Document No. 89:38322 Study of the equilibrium structural mobility of macromolecules according to the luminescence characteristics of protein chromophores. Burshtein, E. A.; Bushueva, T. L.; Permyakov, E. A. (USSR). Zhurnal Prikladnoi Spektroskopii, 28(4), 653-7 (Russian) 1978. CODEN: ZPSBAX. ISSN: 0514-7506.

AB The inverse of the fluorescence quantum yield for tryptophan residues in RNase C2, **human** serum albumin, Escherichia coli L- **asparaginase**, azurin, and neurotoxins I and II of Naja oxiana as well as for tyrosine residues in N. oxiana cytotoxin and carp parvalbumin 3 was a linear function of I/η where I = temperature in K and η = solvent viscosity in cP. The inverse of the fluorescence lifetime of these groups was also a linear function of I/η, as was the relative rate of fluorescence quenching of these groups in L-asparaginase and β-lactoglobulin by KI and in RNase C2 by acrylamide. During a decrease in temperature from 0 to -196°C, the fluorescence spectrum of β-lactoglobulin, possessing only internal tryptophan residues, was gradually shifted to a shorter wavelength at -20 to -90°C, whereas that for N. oxiana neurotoxin I, posessing internal and surface tryptophan residues, was sharply shifted to a shorter wavelength at 0 to -20°C and was shifted to a still

shorter wavelength at -20 to -90°C. Such shifts were not observed in dessicated protein powders. Thus, the fluorescence properties of proteins essentially depend on the fast ns mobility of the protein structures in the chromophore environment, and the spontaneous mobility of protein structures, even those buried in the interior of the mol., depends on the rate of diffusion in the surrounding solvent.

L6 ANSWER 6 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1978:110551 Document No. 88:110551 L-asparaginase preparations for treatment of leukemia. Naito, Ryoichi; Inada, Yuji; Miyake, Shoichi (Green Cross Corp., Japan). Jpn. Kokai Tokkyo Koho JP 52151723 19771216 Showa, 4 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1976-69027 19760612.

AB L-Asparaginase [9015-68-3] prepns. for treatment of leukemia are prepared by spreading L-**asparaginase**-containing **human** fibrins on thrombin-pretreated, thermostable materials such as nylon, polyolefin fibers, polyacrylonitrile fibers, polyester fibers, etc. An apparatus containing the prepns. for use in exogenous circulation is described. The blood concns. of L-asparagine [70-47-3] were 28, 17.6, 5.1 and 0.5 nmol/mL, resp. 0, 60, 140, and 200 min after circulation as determined in dogs.

L6 ANSWER 7 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1978:46962 Document No. 88:46962 **Human** fibrin entrapped L-**asparaginase** and its heat stabilization. Inada, Yuji; Miyake, Shoichi (Green Cross Corp., Japan). Jpn. Kokai Tokkyo Koho JP 52117489 19771001 Showa, 11 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1976-34642 19760329.

AB **Human** fibrin is used to immobilize L-**asparaginase**; hepatitis virus, if present in the fibrin-enzyme preparation, may be inactivated by heating the preparation in an amine (15-150 mM)-containing solution (pH 6.5-9.5) at 55-65° for 9-11 h without inactivating the enzyme activity. Thus, 8 mL of 2.5% human fibrinogen in 20 mM citrate buffer (pH 6.2) containing 25 mM CaCl2 was stirred vigorously and mixed with 1 mg L- **asparaginase**, 0.8 mL **human** thrombin (60 NIH units/mL), and 50 mM glutaraldehyde; a sponge-like fibrin-immobilized L-asparaginase preparation was formed. When the fibrin-L-asparaginase preparation was heated at 60° for 10 h in a solution (pH 6.5-9.5) containing 20 mM glycine, >65% of the initial enzyme activity remained in the heat-treated fibrin-enzyme preparation

L6 ANSWER 8 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1977:513713 Document No. 87:113713 Physicochemical properties of deamidase AG from Pseudomonas fluorescens AG, exhibiting antitumoral activity. Rakov, S. S.; Prozorovskii, V. N.; Grebenshchikova, O. G.; Kondrat'eva, N. A. (Lab. Enzymol., Moscow, USSR). Voprosy Meditsinskoi Khimii, 23(4), 503-8 (Russian) 1977. CODEN: VMDKAM. ISSN: 0042-8809.

AB Homogeneous deamidase from P. fluorescens AG was a glycoprotein with mol. weight of .apprx.130,000 daltons. The mol. is composed of 4 similar or identical subunits with mol. wts. of .apprx.30,000 daltons. The amino acid composition of the deamidase was similar to those of L-asparaginases of other microorganisms. The N-terminal amino acid was lysine and there were 8 carboxymethylcysteine residues/mol. There are apparently 4 disulfide bonds/mol., 1/subunit, which do not play any role in intersubunit binding. The carbohydrate content of the deamidase was estimated at .apprx.9%. The enzyme had a distinct antitumor effect on Burkitt's lymphoma cells, which are asparaginase-sensitive, but had a weak cytotoxic action on cells of **human** ovarian cancer CaOV line, which are **asparaginase** -resistant.

L6 ANSWER 9 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1974:434838 Document No. 81:34838 Immobilized enzymes. Applications in medicine. Anderson, Paul M.; Salo, Wilmar L. (Sch. Med., Univ. Minnesota, Duluth, MN, USA). Minnesota Medicine, 56(12), 1036-40 (English) 1973. CODEN: MIMDAL. ISSN: 0026-556X.

AB A review with 13 refs., on the use of immobilized enzymes as specific catalytic reagents in medicine. The immobilized enzymes are more stable than the corresponding soluble enzymes, can be used repeatedly, and removed easily from the reaction mixture The immobilized derivs. of urease and ureate oxidase are used for the continuous and automated anal. of urea and uric acid. Immobilized enzymes are highly useful in conjunction with an electrochem. probe. Immobilized **asparaginase** is effective in clearing asparagine from **human** blood. In the future, immobilized enzymes may be used for the treatment of enzyme deficiency. They are also useful in the synthesis of medicinals, as models of membranes and metabolic cycles in basic research, and as immunoadsorbents for the isolation of antibodies to the enzymes.

L6 ANSWER 10 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1974:144332 Document No. 80:144332 Effect of L-**asparaginase** and hydrocortisone on **human** lymphocyte transformation and production of a mononuclear leukocyte chemotactic factor in vitro. Ruehl, H.; Vogt, W.; Bochert, Gudrun; Schmidt, Susanne; Moelle, Renate; Schaoua, H. (Klin. Steglitz, Freie Univ. Berlin, Berlin, Fed. Rep. Ger.). Immunology, 26(5), 989-94 (English) 1974. CODEN: IMMUAM. ISSN: 0019-2805.

AB Human peripheral lymphocytes stimulated in vitro with phytohemagglutinin (PHA) produced a soluble factor which is chemotactic for homologous monocytes. Synthesis of this factor preceded the blastogenic response as measured by thymidine-3H incorporation. In cultures of unsepd. leukocytes, maximum chemotactic activity was detected after 24 hr, whereas in supernatants from purified lymphocyte suspensions the maximum synthesis occurred after 72 hr. High doses of L-asparaginase from Escherichia coli which prevented lymphocyte transformation completely had no influence on production of the chemotactic factor. Thus induction of DNA synthesis by PHA and its effect on production of chemotactic factor depend on different biochem. mechanisms. In contrast hydrocortisone induced dose-dependent inhibition of both DNA synthesis and chemotactic response.

L6 ANSWER 11 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1974:25838 Document No. 80:25838 Prolongation of survival of allogenic skin grafts by L-asparaginase. Hammer, C.; Brendel, W. (Surg. Clin., Univ. Munich, Munich, Fed. Rep. Ger.). European Surgical Research, 3(1), 72-5 (English) 1971. CODEN: EUSRBM. ISSN: 0014-312X.

AB L-**Asparaginase** (in dosages recommended for **humans**) prolonged the survival of allogeneic skin transplants in rats. It was less effective than other immunosuppressants, i.e., corticoids, azathioprine, or antilymphocyte globulin. Since administration of asparaginase resulted in heavy loss (.apprx.30%) of body weight, increasing the dosage to improve effectiveness was not advisable. No difference in the immune response was observed when the animals were treated with asparaginase prior to grafting.

L6 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1973:11970 Document No. 78:11970 Inhibition of protein and nucleic acid syntheses by Escherichia coli L-**asparaginase** in sensitive and resistant mouse leukemias, **human** leukemia cells, and normal human lymphocytes. Benvenisti, Dan S.; Burchenal, Joseph H.; Ochoa, Manuel, Jr. (Div. Appl. Ther., Sloan-Kettering Inst. Cancer Res., New York, NY, USA). Oncol., Proc. Int. Cancer Congr., 10th, Meeting Date

1970, Volume 2, 97-104. Editor(s): Clark, R. Lee. Yearb. Med.: Chicago, Ill. (English) 1971. CODEN: 25NIAK.

AB A discussion and review with no refs. of the in vitro inhibitory effects of L-asparaginase [9015-68-3] on the syntheses of protein and nucleic acids in cells sensitive and resistant to the enzyme.

L6 ANSWER 13 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1972:456454 Document No. 77:56454 Inactivation of complement by L-asparaginase preparations not correlated with enzyme content. Comments. Loos, M.; Borsos, T. (Biol. Branch, Natl. Cancer Inst., Bethesda, MD, USA). Nature (London), New Biology, 237(71), 55-6 (English) 1972. CODEN: NNBYA7. ISSN: 0369-4887.

AB Neither of 2 L-asparaginase [9015-68-3] prepns. destroyed guinea pig complement activity. One of the prepns. fixed only a small amount of human complement in human sera while the other fixed all measurable complement in human sera. Activation of C1 by a given lot of L-**asparaginase** depended on the source of **human** serum. A small reduction in late component activity was observed in human sera exposed to the prepns. The effects on **human** complement of L-**asparaginase** prepns. appear to be due to a contaminant present in different quantities in different lots of L-asparaginase.

L6 ANSWER 14 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1972:148692 Document No. 76:148692 Distribution and elimination of administrered L-asparaginase. Putter, J. (Inst. Exp. Pathol., Farbenfabr. Bayer A.-G., Wuppertal, Fed. Rep. Ger.). Colloques Internationaux du Centre National de la Recherche Scientifique, No. 197, 389-94 (English) 1971. CODEN: COINAV. ISSN: 0366-7634.

AB L-asparaginase (I) [9015-68-3] administered i.v. into mice was primarily localized in the blood plasma, but later could be detected in the whole body. The elimination rate of I from the plasma paralleled that of the whole body, and approximated 1st order kinetics with a half-life-time (HLT) of 3 hr. The elimination rates of L-asparaginase A (Crasnitin) [9015-68-3] (a natural enzyme from Escherichia coli) and L- **asparaginase** X [9015-68-3] (artificial isoenzyme), differed in **human** but not in other animal species; however cats showed approx. the same results as man. When the elimination rates of various modified I were studied in cats, only acetyl asparaginase [9037-23-4] had a higher biol. HLT than L-asparaginase X.

L6 ANSWER 15 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1972:121532 Document No. 76:121532 Comparison of the adriamycin and L-**asparaginase** effects on **human** lymphocytes in cell-culture. Astaldi, A., Jr.; Curtoni, E.; Ugazio, A.; Mingrat, G. (Pediatr. Clin., Univ. Med. Sch., Pavia, Italy). Blut, 23(6), 367-72 (English) 1971. CODEN: BLUTA9. ISSN: 0006-5242.

AB Adriamycin (I) [23214-92-8] inhibited blastogenesis of human lymphocytes in a phytohemagglutinin-stimulated culture by a cytotoxic mechanism that kills the cells, whereas L-asparaginase inhibited blastogenesis by depriving lymphocytes of L-asparagine [70-47-3], which is essential for their activation and growth, without any cellular damage.

L6 ANSWER 16 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1971:474123 Document No. 75:74123 Effect of L-asparaginase in mixed leukocyte culture. Shons, Alan R.; Etheredge, Edward E.; Najarian, John S. (Dep. Surg., Univ. Minnesota, Minneapolis, MN, USA). Transplantation, 12(1), 85-7 (English) 1971. CODEN: TRPLAU. ISSN: 0041-1337.

AB L-**Asparaginase**, an immunosuppressor, inhibits blastogenesis in mixed **human** leukocyte cultures. With a weakly reacting pair of leukocytes, (HL-A9, 7, 4b) x (HL-A1, 2, 7, 8 and Te 57), complete inhibition occurred at all concns. examined (1.0, 5, and 10 IU/ml), and addition of high concns. of asparagine, glutamine, or aspartic acid did not reverse the inhibition. With a strongly reacting pair, (HL-A1, 3, 7) x (HL-A12, 4a), inhibition occurred at 10 IU/ml, but at 0.1 and 1.0 IU/ml some stimulation occurred; addition of amino acids did not reverse the inhibition. The stimulation may be due to the antigenic potential of the enzyme. The inhibition apparently is not related to a direct toxic effect on the cells. The mechanism of L-asparaginase immunosuppression remains to be proved. Blastogenesis was measured by the uptake of thymidine-H by the cells in culture.

L6 ANSWER 17 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:415251 Document No. 75:15251 Asparaginase used to treat leukemia. Waid, G. E.; Ratter, D. A. (UK). Priroda (Moscow, Russian Federation) (12), 32-5 (Russian) 1970. CODEN: PRIRA3. ISSN: 0032-874X.
AB The mechanism of action of **asparaginase** in the treatment of **human** leukemia was discussed.

L6 ANSWER 18 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:403351 Document No. 75:3351 L-Asparaginase and proliferative activity of the PHA- [phytohemagglutinin] stimulated lymphocytes. Krc, Ivo; Astaldi, Alberto, Jr.; Astaldi, Giovanni; Krcova, Vera; Ugazio, A.; Mistretta, A. P. (Blood Res. Found. Cent., Hosp. Tortona, Tortona, Italy). Bollettino dell'Istituto Sieroterapico Milanese, 49(6), 515-19 (Italian) 1970. CODEN: BISMAP. ISSN: 0021-2547.
AB L-**Asparaginase** intensely inhibits blastic transformation of **human** peripheral blood lymphocytes in the PHA-stimulated cultures. The problem of whether the enzyme also influences mitotic division of blastic transformed cells was studied. Different concns. of L-asparaginase were added to the PHA-cultivated cells at the 66th hr of cultivation. The controls showed normal blastogenesis. After 72 hr of culture, the mitotic indexes were determined on May-Grunwald-Giemsa treated smears. L-Asparaginase inhibits mitotic activity of the blastlike cells in culture, but does not interfere with the cytodiaresis of the cells which have entered the mitotic stage at the time of addition of L-asparaginase.

L6 ANSWER 19 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:74527 Document No. 74:74527 L-**Asparaginase** and **human** malignant disease. Crowther, D. (St. Bartholomew's Hosp., London, UK). Nature (London, United Kingdom), 229(5281), 168-71 (English) 1971. CODEN: NATUAS. ISSN: 0028-0836.
AB A review with 50 refs.

L6 ANSWER 20 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:51849 Document No. 74:51849 Effect of L-asparaginase on the synthesis and processing of ribosomal precursor RNA in PHA-[phytohemagglutinin] stimulated lymphocytes. Torelli, Umberto L.; Torelli, Giuseppe M.; Andreoli, Antonio; Mauri, Carlo (Inst. Med. Pathol., Univ. Modena, Modena, Italy). Experientia, 26(12), 1366-8 (English) 1970. CODEN: EXPEAM. ISSN: 0014-4754.
GI For diagram(s), see printed CA Issue.
AB One of the earliest effects of L-asparaginase in L-asparaginase-sensitive cells is the impairment in synthesis and processing of ribosomal precursor RNA. In vitro, tritiated uridine (I) incorporation into phytohemagglutinin-

stimulated **human** lymphocytes was markedly inhibited by L-**asparaginase**. A relevent proportion of the radioactivity was associated with the 45 S RNA, even after 3 hr of incubation with the precursor.

L6 ANSWER 21 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:41054 Document No. 74:41054 Resistance to L-**asparaginase** in **human** leukemia. Canellos, George P.; Haskell, Charles M. (Med. Branch, Natl. Cancer Inst., Bethesda, MD, USA). Recent Results in Cancer Research, 33, 188-93 (English) 1970. CODEN: RRCRBU. ISSN: 0080-0015.
AB Asparagine synthetase (I) activity was negligible in leukemic cells from 18 patients before and in 9 cases during or after asparaginase (II) treament. I activity increased 7-fold in patients unresponsive to treatment. Every patient refractory to II showed a significant increase in I activity. Myelotoxicity did not occur with II treatment. Normal marrow from patients with nonhemopoietic neoplasms treated with II showed I activity increases similar to those of resistant leukemic cells. I activity was inhibited by II derived from leukemic leukocytes.

L6 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:40990 Document No. 74:40990 Pharmacokinetic behavior of L-asparaginase in men and in animals. Puetter, Johann (Inst. Exp. Pathol., Farbenfabr. Bayer A.-G., Wuppertal-Elberfeld, Fed. Rep. Ger.). Recent Results in Cancer Research, 33, 64-74 (English) 1970. CODEN: RRCRBU. ISSN: 0080-0015.
AB The rate of elimination of asparaginase-A from blood plasma was found to differ widely in different species, the elimination approx. following 1st-order kinetics. In **humans**, the elimination of **asparaginase**-A from the blood had a half-life of 12 hr while that of asparaginase-X was 24 hr. In healthy and tumor-bearing mice, exogenous asparaginase-A was demonstrated in all organs except the brain. After repeated injections of asparaginase-A (300 IU/kg) into dogs and rabbits at intervals of several days, its elimination was greatly accelerated. It is suggested that this acceleration was due to antibody formation.

L6 ANSWER 23 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:40836 Document No. 74:40836 Inhibition by L-**asparaginase** from E[scherichia] coli of **human** malignant melanoma cells growing in vitro. Alexander, Peter; Fairley, G. Hamilton; Hunter-Craig, I. D.; Ilonopisov, R. L.; Lewis, M. G. (Chester Beatty Res. Inst., Belmont/Sutton/Surrey, UK). Recent Results in Cancer Research, 33, 151-4 (English) 1970. CODEN: RRCRBU. ISSN: 0080-0015.
AB Malignant melanoma cells were cultured in the presence of E. coli L-asparaginase (I). I inhibited 30% of the 60 malignant melanomas in vitro. Eleven of the 15 sensitive tumors were inhibited by 5 μg I/ml; 4 required 20-40 μg I/ml. No correlation existed between sensitivity to I and the immune reactivity against the melanoma cells. In vitro sensitivity to I occurred in the same proportion among patients with and without autoantibodies. Neither asparagine (II)-sensitive or II-resistant cells required II for growth. The effects of E. coli I may be wholly or partially due to glutamine deprivation.

L6 ANSWER 24 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1971:30390 Document No. 74:30390 Inhibition of the cytoaggressive effect of phytohemagglutinin (PHA)-stimulated **human** lymphocytes by E[scherichia] coli L-**asparaginase** (EC-2-A-SE). Oerkermann, H.; Hirschmann, W. D.; Schumacher, Kurt; Alzer, G.; Uhlenbruck, Gerhard; Gross, Rudolf (Med. Universitaetsklin. Koeln-Lindenthal,

Cologne-Lindenthal, Fed. Rep. Ger.). Klinische Wochenschrift, 48(22), 1368-9 (English) 1970. CODEN: KLWOAZ. ISSN: 0023-2173.

AB The PHA-stimulated transformation of human lymphocytes into blast-like cells, and their destructive effect on HeLa cells in vitro, was inhibited by L-asparaginase.

L6 ANSWER 25 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:464623 Document No. 73:64623 Effect of immunodepressants on the lymphocyte membrane. Beretta Anguissola, Alessandro; Lajolo di Cossano, Donatella; Pecco, P.; Bert, C. (Italy). Revista Clinica Espanola, 116(6), 531-4 (Spanish) 1970. CODEN: RCESA5. ISSN: 0014-2565.

AB Antilymphocytic globulin, prednisolone, and, to a lesser degree, L-**asparaginase**, retarded the electrophoretic migration of **human** lymphocytes from the peripheral blood, whereas vinblastine had no effect.

L6 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:443526 Document No. 73:43526 Effect of L-asparaginase on the blastic transformation of normal lymphocytes. Marras, F.; Franzosi, P.; Taglioretti, D.; Cardana, R. (Osp. "C. Ondoli", Angera, Italy). Haematologica Latina, 12(2), 135-41 (Italian) 1969. CODEN: HALAAW. ISSN: 0017-6575.

AB The effects of L-**asparaginase**(I) on cultures of normal **human** leukocytes were studied. In low concns. (5 and 30 IU/ml medium) I inhibited the proliferation of blast cells, but had no significant effect on the transformation of lymphocytes to blasts. High concns. (60 IU/ml), however, completely inhibited the development of lymphocyte cultures.

L6 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:443319 Document No. 73:43319 Failure of Escherichia coli L-asparaginase to produce acute pancreatitis in sensitized guinea pigs and in rabbits given daily I.V. doses. Rakieten, Nathan; Cooney, David A.; Davis, Ruth D. (South Shore Anal. and Res. Lab., Inc., Islip, NY, USA). U.S. Clearinghouse Fed. Sci. Tech. Inform., PB Rep., No. 189327, 6 pp. Avail. CFSTI From: U. S. Govt. Res. Develop. Rep. 1970, 70(7), 50 (English) 1970. CODEN: XCCRAO.

AB Studies were undertaken to develop a model for Escherichia coli L-**asparaginase** pancreatitis which is reported occasionally in **humans**. No evidence of pancreatitis was ever seen in monkeys, dogs, rabbits, and guinea pigs treated with L-asparaginase so it was decided to determine whether acute pancreatitis would occur in guinea pigs sensitized to L-asparaginase and in rabbits receiving repeated doses of L-asparaginase. None of the procedures produced any histopathol. evidence of pancreatitis in either species. Further at the dose level administered to rabbits, 1,000 IU/kg/day + 11, i.v. there were no significant changes in blood sugar or plasma amylase in the animals. The rabbits treated with L-asparaginase showed evidence of hemagglutination antibodies, but this was complicated by the fact the controls also showed antibodies.

L6 ANSWER 28 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:442929 Document No. 73:42929 Inhibitory effect of L-asparaginase in lymphocyte transformation induced by phytohemagglutinin. Miura, Moriji; Hirano, Masami; Kakizawa, Kumi; Morita, Akimitsu; Uetani, Tadaaki; Yamada, Kazumasa (Sch. Med., Nagoya Univ., Nagoya, Japan). Cancer Research, 30(3), 768-72 (English) 1970. CODEN: CNREA8. ISSN: 0008-5472.

AB The effect of Escherichia coli L-**asparaginase** on phytohemagglutinin (PHA)-induced transformation of **human** lymphocytes was studied. Transformation was

remarkably suppressed by the enzyme when it was added to the culture not later than 24 hr after its initiation. The effective concentration was >0.2 IU/tube. Guinea pig serum and L-β-aspartohydroxamic acid, an L-asparagine analog, have a suppressive effect on lymphocyte transformation in this system. PHA-treated lymphocytes became sensitive to L-asparaginase 12 hr after the culture was started, while no L-asparagine dependency was detected at any stage of the culture. An addition of L-asparagine or L-glutamine to the culture system treated with both PHA and L-asparaginase at zero time caused the partial recovery of thymidine-3H uptake. Thus, it is concluded that 1 of the mechanisms inhibiting PHA lymphocyte transformation by L-asparaginase is due to the deprivation of exogenous L-asparagine and L-glutamine from the tissue culture medium.

L6 ANSWER 29 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:433642 Document No. 73:33642 Reversal by L-glutamine of the inhibition of lymphocyte mitosis caused by Escherichia coli asparaginase. Simberkoff, Michael S.; Thomas, Lewis (Sch. of Med., New York Univ., New York, NY, USA). Proceedings of the Society for Experimental Biology and Medicine, 133(2), 642-4 (English) 1970. CODEN: PSEBAA. ISSN: 0037-9727.

AB Inhibition of **human** lymphocyte mitosis by Escherichia coli L- **asparaginase** can be prevented by addition of L-glutamine to enzyme-treated culture medium. Like arginine, glutamine appears to be essential for lymphocyte transformation and mitosis, while exogenous asparagine is not required.

L6 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:423362 Document No. 73:23362 L-asparagine requirement and the effect of L-**asparaginase** on the normal and leukemic **human** bone marrow. Ho, Dah Hsi Wang; Whitecar, John P., Jr.; Luce, James K.; Frei, Emil, III (M. D. Anderson Hosp. and Tumor Inst., Houston, TX, USA). Cancer Research, 30(2), 466-72 (English) 1970. CODEN: CNREA8. ISSN: 0008-5472.

AB The bone marrow of patients with acute lymphocytic leukemia and acute myelogenous leukemia, and normal bone marrow all showed L-asparagine (I) dependence. There was a direct correlation between the concentration of L-asparaginase (II) and depression of cell function in vitro. These results were consistent with the initial antileukemic effect of II. Activity of I-synthetase (III) was low but there was no correlation between III and the production of remission by II. In a preliminary study of serial determination of the in vitro test and III activity of the bone marrow during treatment with II, a decreasing I requirement and an increasing III activity were observed

L6 ANSWER 31 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1970:413068 Document No. 73:13068 Lymphocyte suppressive effect of Escherichia coli L-asparaginase. Biscatti, Giuliano; Astaldi, Alberto, Jr.; Ferfoglia, Luciano; Burgio, G. Roberto; Astaldi, Giovanni (Pediat. Clin., Univ. Med. Sch. Pavia, Pavia, Italy). Bollettino dell'Istituto Sieroterapico Milanese, 48(5), 502-6 (English) 1969. CODEN: BISMAP. ISSN: 0021-2547.

AB A single injection of E. coli L-**asparaginase** was administered i.v. to **humans** (200-800 IU/kg) and peripheral blood lymphocytes were incubated in a phytohemagglutinin (PHA) culture medium, to test the inhibiting action of asparaginase on blastogenesis. A rather long lasting inhibition was observed; blastogenesis reached the normal value only 10-14 days after the treatment. In a 2nd experiment, PHA cross-cultures were set up with lymphocytes from subjects injected i.v. with E. coli L-asparaginase, plus serum from noninjected subjects, and vice-versa. Results indicated that lymphocytes from asparaginase-injected subjects do not lose their capacity for blastogenesis in

cell culture. In fact it was only the addition of serum from asparaginase-injected subjects to the culture that caused the blastogenesis inhibition of lymphocytes from both asparaginase injected and noninjected subjects.

L6 ANSWER 32 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1970:412698 Document No. 73:12698 L-asparaginase and L-asparagine metabolism. Cooney, David A.; Handschumacher, R. E. (Lab. of Toxicol., Nat. Cancer Inst., Washington, DC, USA). Annual Review of Pharmacology, 10, 421-40 (English) 1970. CODEN: ARVPAX. ISSN: 0066-4251.
AB A review is presented. At present the therapeutic efficiency of L-**asparaginase** (I) in the treatment of **human** disease appears to be limited to the prompt induction of remission in both virgin and veteran cases of acute lymphocytic leukemia, but this enzyme has engendered a major interest in the potential use of other enzymes in the theory of human disease. The unique nutritional requirement of some cells for I requires further study. 166 refs.

L6 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1970:402585 Document No. 73:2585 Asparaginase--treatment for leukemia. Wade, H. E.; Rutter, D. A. Science Journal, 6(3), 62-7 (English) 1970. CODEN: SCJUAD. ISSN: 0582-2092.
AB About 30% of mouse tumors treated with asparaginase regressed. As a source of quantities of **asparaginases** large enough for treatment of **human** beings, Escherichia coli was used, but some asparaginases were inactive. Under laboratory conditions, a remission rate of 60% was obtained for acute lymphatic leukemia, with slight-side effects. All these cases later relapsed, but, by the use of prednisone and vincristine to induce a remission and asparaginase to maintain it, some lives were prolonged.

L6 ANSWER 34 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1970:130753 Document No. 72:130753 L-**asparaginase**, an inhibitor of **human** lymphocyte transformation. Astaldi, Giovanni; Burgio, G. Roberto; Krc, Ivo; Astaldi, Alberto, Jr.; Krcova, Vera; Genova, Roberto (Blood Res. Found. Center, Tortona, Italy). Medizinische Klinik (Muenchen, Germany), 65(10), 451-4 (German) 1970. CODEN: MEKLA7. ISSN: 0723-5003.
AB L-Asparaginase (I) was first found in guinea pig serum. It caused degradation of L-asparagine (II) and glutamine. The inhibition of cell growth by I was determined in vivo in animals and in human leukemia. Cultures of lymphocytes (sterile heparinized venous blood) were incubated 72 hr in a medium with phytohemagglutinin (III) or I or a mixture of both. Cultures without III, with or without I showed no significant transformation of lymphocytes. In III containing cultures an inhibition can be observed already at 0.01-0.1 units of I per ml, optimum at 1.0 per ml. The inhibition started on addition of the enzyme. The tests suggested that I not only inhibited pathol. cell systems (which cannot synthesize I), but also normal lymphocytes, and that II and glutamine were necessary for the transformation. It was not elucidated whether the inhibition was a toxic or enzymic effect.

L6 ANSWER 35 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1970:10905 Document No. 72:10905 1-**Asparaginase** resistance in **human** leukemia. Asparagine synthetase. Haskell, C. M.; Canellos, G. P. (Med. Br., Nat. Cancer Inst., Bethesda, MD, USA). Biochemical Pharmacology, 18(10), 2578-80 (English) 1969. CODEN: BCPCA6. ISSN: 0006-2952.
AB Determination of asparagine synthetase (I) was made in cells from bone marrow aspirate or peripheral blood specimens obtained by plasmapheresis in 18

leukemic patients who were then treated with 200 IU/k/day of asparaginase (II) from E. coli. Duration of treatment was 3 weeks except for 1 patient who showed both toxicity and response in 3 days. Prior to therapy and regardless of response, I was nearly undetectable. In 4 patients who responded to treatment, there was no change in I with therapy but in 5 patients who were unresponsive, there was 7-fold increase in the mean level of I. The data indicate that resistance to II in human leukemic cells is at least partly related to the capacity for biosynthesis of asparagine via I.

L6 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1969:479428 Document No. 71:79428 Effect of L-asparaginase on the ability of normal mouse bone marrow to form soft agar colonies. Harris, Jules E. (Ottawa Gen. Hosp., Ottawa, Can.). Nature (London, United Kingdom), 223(5208), 850-1 (English) 1969. CODEN: NATUAS. ISSN: 0028-0836.
AB Previous studies have shown that L-**asparaginase**, an enzyme thought to selectively inhibit **human** tumor cells requiring asparagine, may have toxic side effects which arise from action on normal cells. Therefore, the effects of L-asparaginase (10-1000 I.U., i.p.) on colony formation by mouse bone-marrow cells, which are closely related to hematopoietic stem cells, in soft agar were studied. As little as 10 I.U. L-asparaginase inhibited colony formation, and this effect was not reversed by 20 or 40 mg. of asparagine supplements. However, asparagine increased colony-formation inhibited in cells from mice pretreated with 100 or 1000 I.U. of the enzyme. Thus, L-asparaginase does affect normal myeloid cells.

L6 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1969:458891 Document No. 71:58891 Influence of human serum on the antitumor activity of two L-asparaginases. Lee, Maureen B.; Niblock, Rosalie M.; Bridges, John M. (Roy. Victoria Hosp., Belfast, Ire.). British Journal of Cancer, 23(2), 369-76 (English) 1969. CODEN: BJCAAI. ISSN: 0007-0920.
AB Mice injected s.c. with leukemia cells (system EARAD/1) received graded doses of asparginase from guinea pig serum or from E. coli, alone or with human serum. Although E. coli asparaginase was most effective if given simultaneously with the tumor cells and with **human** serum, the antitumor activity of **asparaginase** from guinea pig serum was not affected by addition of human serum.

L6 ANSWER 38 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1969:429218 Document No. 71:29218 Hypoalbuminemic and hypocholesterolemic effect of L-asparaginase (NSC-109,229) treatment in man. Canellos, G. P.; Haskell, C. M.; Arseneau, J.; Carbone, P. P. (Nat. Cancer Inst., Public Health Serv., Bethesda, MD, USA). Cancer Chemotherapy Reports, 53(1), 67-9 (English) 1969. CODEN: CNCRA6. ISSN: 0069-0112.
AB When 6 patients with nonleukemic metastatic neoplasms were treated with L-asparaginase (200 I.U./kg./day i.v. for 10-21 days), the serum albumin levels of 5 of the 6 patients decreased to 30-50% of pretreatment levels within 14 days of therapy. Total globulin changes were less pronounced, but in most cases decreased from initial levels. The cholesterol levels also decreased during the therapy. The hypoalbuminemic and hypocholesterolemic effects improved after the cessation of therapy. Studies in vitro with L-**asparaginase** did not demonstrate an effect on **human** serum proteins. These effects of the L-asparaginase treatment may be due to L-asparagine depletion with concomitant disruption in the hepatic synthesis of proteins.

L6 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1969:113299 Document No. 70:113299 Asparagine synthetase activity in

malignant and nonmalignant human kidney and prostate specimens. Prager, Morton D.; Peters, Paul C.; Janes, Jefferson O.; Derr, Ina (Southwestern Med. Sch., Univ. of Texas, Dallas, TX, USA). Nature (London, United Kingdom), 221(5185), 1064-5 (English) 1969. CODEN: NATUAS. ISSN: 0028-0836.

AB Susceptibility of **human** tumors to the inhibitory action of **asparaginase** (I) was studied. Tests were made on samples of kidney (cortex and medulla) and prostate to determine the levels of asparagine synthetase (II) in a variety of malignant and nonmalignant tissues. A wide range of values was observed for the latter specimens and only 2 out of 16 failed to exhibit II activity. Only 2 out of 8 specimens from renal-cell tumors had detectable II activity. In 4 of 6 malignant specimens paired with samples from nonmalignant kidney of the same patient the nonmalignant biopsy had II activity and none was detected in the tumor. This biochem. difference in the activity of II between malignant and nonmalignant kidney samples suggested that these tumors may be susceptible to the action of I. II assays showed that there was little or no II in either malignant or nonmalignant prostate specimens.

L6 ANSWER 40 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1969:66729 Document No. 70:66729 Inhibition of **human** malignant neoplasia by L-**asparaginase**. Oettgen, Herbert F.; Schulten, Hans K. (Sloan-Kettering Inst. for Cancer Res., New York, NY, USA). Klinische Wochenschrift, 47(2), 65-71 (German) 1969. CODEN: KLWOAZ. ISSN: 0023-2173.

AB Eighty-eight patients with various malignant diseases were treated with L-asparaginase (I) prepared from Escherichia coli. Daily I doses given were ≤5000 I.U./kg. body weight Therapeutic results were evaluated in 60 patients. Bone marrow remissions were obtained in 20 of 35 patients with acute lymphoblastic leukemia, in 1 with lymphosarcoma in the leukemic phase, and in 1 of 5 with acute myeloor myelomonoblastic leukemia; the remissions lasted 1-8 months. Of 21 with malignant lymphomas, sarcomas, or carcinomas, only 1 patient (with malignant melanoma) responded to treatment with I. No bone marrow depression was observed with these I doses. Side effects were few and reversible. The effect of I on neoplastic cells was also demonstrated in vitro; this test, however, can as yet not be used to predict therapeutic results. In cases where resistance developed during I treatment of primarily I sensitive leukemia, leukemic cells no longer required asparagine (II) in vitro. Metabolic pathways for synthesizing II by cells resistant to I are discussed.

L6 ANSWER 41 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN

1968:75332 Document No. 68:75332 L-**Asparaginase** activity in **human** animal sera. Lee, Maureen B.; Bridges, John M. (Roy. Victoria Hosp., Belfast, UK). Nature (London, United Kingdom), 217(5130), 758-9 (English) 1968. CODEN: NATUAS. ISSN: 0028-0836.

AB An outstanding characteristic of L-asparaginase (I) is its ability to inhibit the growth of certain rodent leukemias and some favorable response in human leukemias. I can be extracted from guinea pig serum and also from certain types of Escherichia coli; I from the latter occurs in 2 forms with widely differing biol. activities. I activity was not detected in human sera nor in sera from horse, cow, pig, sheep, dog, monkey, rabbit, and chicken. When human sera were combined with guinea pig sera the I activity was enhanced, but the degree of enhancement did not correspond to the initial I content. None of the animal sera tested produced results, except that of sheep and 1 pig; sheep serum consistently enhanced the I activity of guinea pig serum. However, the addition of all human and animal sera increased the I activity of the coliform extract By ultrafiltration the protein fraction from human serum

was concentrated The I-enhancing effect was contained in the protein moiety, while the protein-free fraction had no effect. 18 references.

L6 ANSWER 42 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1967:488983 Document No. 67:88983 Glutaminase and asparaginase activity in normal tissues and malignant tumors. Berezov, T. T. (Univ. Druzhby Narodov Im. Lumumby, Moscow, USSR). Ukrains'kii Biokhimichnii Zhurnal (1946-1977), 38(5), 484-9 (Russian) 1966. CODEN: UBZHAZ. ISSN: 0372-3909.

AB Homogenates of primary human tumors (gastric, intestinal, hepatic, and mammary carcinoma) and exptl. animal tumors (mouse C3HA hepatoma, rat hepatoma, rhabdomyosarcoma, and sarcoma, and rabbit Brown-Pearce carcinoma) as well as those of corresponding normal tissues were incubated in a phosphate buffer, pH 8.0, with arsenite and glutamine or asparagine for 2 hrs. Ammonia liberated during incubation was determined by the Conway method. In all **human** tumors studied both glutaminase (I) and **asparaginase** (II) activity was much lower than in control tissues. In intestinal tumor tissue no II activity was detected. Normal I activity was found in all animal tumors studied. Measurable II activity was demonstrated only in the Brown-Pearce tumor at 14% the level in control testicles. No II was found in rat and mouse hepatomas. It is concluded that tumors are characterized by a specific enzymic pattern which is different from that of corresponding normal tissues.

L6 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1967:53663 Document No. 66:53663 L-**Asparaginase**: toxicity to normal and leukemic **human** lymphocytes. Schrek, Robert; Dolowy, William C.; Ammeraal, Robert N. (Tumor Res. Lab., Veterans Admin. Hosp., Hines, IL, USA). Science (Washington, DC, United States), 155(3760), 329-30 (English) 1967. CODEN: SCIEAS. ISSN: 0036-8075.

AB Quant. in vitro tests showed that purified prepns. of L-asparaginase from Escherichia coli were more toxic to blood lymphocytes from 12 of 15 patients with chronic lymphocytic leukemia than to lymphocytes from 25 persons with normal hemograms. Incubation for 7 days with 10 units/ml. killed, on the average, 77% of leukemic and 34% of normal lymphocytes. The reagent produced appreciable toxicity to leukemic lymphocytes after 2 days of incubation. 22 references.

L6 ANSWER 44 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1960:86918 Document No. 54:86918 Original Reference No. 54:16545f-i,16546a Amino acid metabolism of mycobacteria. **Asparaginases** and transaminases in **human** tubercle bacilli types H37Rv and H37a, the Vall.acte.ee bovine type, the Griffith avian type, and saprophytic Mycobacterium phlei 61. Ionesco-Mihaiesti, C.; Damboviceanu, Aristie; Vainer, Henriette (Inst. Cantacuzino, Bucharest, Rom.). Arch. roumaines pathol. exptl. et microbiol., 18, 323-45 (French) 1959.

AB cf. CA 52, 2237c. Asparaginase and 3 forms of transaminases were studied in Sauton's medium in the series of decompns. in the sequence asparagine, aspartic acid, glutamic acid, and alanine. Data are given on the enzyme activities of the different types and strains at different time intervals. Enzymic differences were found in the BCG strain and the virulent Vall.acte.ee strain from which it was derived. The virulent human H37Rv strain showed greater biol. and biochem. activity than the attenuated H37a strain derived from it. The Griffith avian strain differed from the bovine and human strains in possessing no amidases, reductases, or nucleases. It also differed in the activities of the 3 transaminases common to all the tubercle organisms, and hydrolyzed asparagine at a slower rate. Mycobacterium phlei 61 also showed differences in enzymic activity, and was deficient in 2 of the 3

transaminases. Amino acids (named) which appeared in cultures of the different strains were identified by paper chromatography. The saprophytic strains generally showed more enzymic activity than the pathogenic strains. This activity reached a maximum after 10-28 days culturing and thereafter declined. Attenuation of virulence does not necessarily involve a loss of enzyme activity. Outstanding enzyme activities were a trypsin-type protease in H37Rv, a nucleotidase in the Vall.acte.ee strain and also in a saprophytic Grassberger 55 strain from milk, and an intense dehydrogenase in M. phlei 61 which is found to a lesser extent in some other strains. 16 references.

L6 ANSWER 45 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
1959:35581 Document No. 53:35581 Original Reference No. 53:6390i,6391a Ammonia excretion and renal enzymic adaptation in human subjects, as disclosed by administration of precursor amino acids. Madison, Leonard L.; Seldin, Donald W. (Univ. of Texas, Dallas). Journal of Clinical Investigation, 37, 1615-27 (Unavailable) 1958. CODEN: JCINAO. ISSN: 0021-9738.
AB In the **human** kidney, glutaminase, **asparaginase**, glycine oxidase, L-amino acid oxidase, and D-amino acid oxidase adapt to chronic acid loads, whereas glutamic dehydrogenase, proline oxidase, and aspartic transaminase do not. 36 references.

=> S L5 NOT L6
L7 93 L5 NOT L6

=> D 1-93 TI

=> D L7 4,12,46,53,54,67,71,72,79 CBIB ABS

L7 ANSWER 4 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1979:504492 Document No. 91:104492 Derivatives of L-**asparaginase** designed to be immobilized in vivo. Mattarella, Nina; Richardson, Tom (Babcock Hall, Univ. Wisconsin, Madison, WI, USA). Biochemical Society Transactions, 7(1), 66-9 (English) 1979. CODEN: BCSTB5. ISSN: 0300-5127.
AB L-**Asparaginase** (I) activity from Escherichia coli decreased with the increased introduction of active groups until 2 mol of p-benzoquinone (II) were incorporated into each mol of I, at which time activity was nearly constant Subsequent coupling of the I derivs. to **human** erythrocytes indicated that 32.9% of the original activity was retained on the cells with a specific activity of 2.38 + 10-8 IU/cell. Recovered activity from the pooled washes of erythrocytes treated with control I and II-I adducts indicated that the latter had been coupled to the erythrocytes. Packed cell vols. increased from 26.5 to 31.3% in washed cells and cells treated with adducts, resp. Erythrocytes treated with control I had a packed cell volume of 29%, indicating some swelling of erythrocytes occurred in cells coupled with I. The osmotic hemolysis of both the II-I adduct- and control I-treated cells was greater than normal, but cells untreated with I also showed similar osmotic fragility. Thus, the observed changes were not due to derivative formation.

L7 ANSWER 12 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1978:44791 Document No. 88:44791 Inhibitory effects of L-**asparaginases**, EC-1 and -2, on blastogenesis of **human** lymphocytes in vitro. Kimm, Seung-Won (Coll. Med., Seoul Natl. Univ., Seoul, S. Korea). Korean Journal of Biochemistry, 8(2), 37-44 (English) 1976. CODEN: KJBID3. ISSN: 0378-8512.
AB L-**Asparaginase** (EC 3.5.1.1) [9015-68-3] was isolated from Escherichia coli, purified by (NH4)2SO4 precipitation, and resolved by DEAE-cellulose column chromatog. into 2 isoenzymes, EC-1 and EC-2. Both isoenzymes inhibited

phytohemagglutinin-induced lymphocyte blastogenesis, as measured by thymidine-3H incorporation. However, EC-2 had a more potent inhibitory effect on blastogenesis than EC-1, and this may relate to the differences in antitumor effects between EC-1 and EC-2 **asparaginases**.

L7 ANSWER 46 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1972:123258 Document No. 76:123258 Asparagine, **asparaginase**, and tRNA. Gallo, Robert C.; Adamson, Richard H. (Natl. Inst. Cancer, Natl. Inst. Health, Bethesda, MD, USA). Colloques Internationaux du Centre National de la Recherche Scientifique, No. 197, 121-32 (English) 1971. CODEN: COINAV. ISSN: 0366-7634.
AB The effect of asparaginyl-tRNA on L-asparagine-sensitive (L5178Y and 6C3HED) repressed asparagine synthetase mouse leukemias, and on L- **asparaginase** resistant (L1210 and 6C3HED/R) depressed asparagine synthetase mouse and **human** leukemic cells (NC-37 and F-152) was studied. For the 2 types of cells, rate and amount of asparaginyl-tRNA formed seemed identical but slightly higher with 6C3HED. Elution profiles of the complexes by freon reverse phase partition chromatog. were compared, and the position, magnitude, and nature of characteristic peaks established. Some L-asparagine-sensitive cells appeared to have higher tRNA acceptor activity than resistant ones.

L7 ANSWER 53 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1971:433960 Document No. 75:33960 L-**Asparaginase**. Rudescu, Karin; Szabados, Judith; Soru, Eugenia (Romania, Institute of Microbiology, Parasitology and Epidemiology "Dr. I. Cantacuzino"). Rom. RO 52461 19710114, 3 pp. (Romanian). CODEN: RUXXA3. APPLICATION: RO 19690904.
AB L-**Asparaginase** was extracted from a nonpathogenic Calmette-Guerin strain of Mycobacterium tuberculosis used for **human** antituberculous vaccination. The exts., prepared in the usual manner, were purified by column chromatog. on Bio-Gel P-200 and Bio-Gel P-10, followed by adsorption on Sephadex G-75 for stabilization.

L7 ANSWER 54 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1971:403921 Document No. 75:3921 Preparations based on L-**asparaginase**. Brown, Harry Darrow (Cancer Research Center). Ger. Offen. DE 2036180 19710225, 34 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1970-2036180 19700721.
AB Insol. L-**asparaginase** (I) is prepared by refluxing 10 g carboxymethyl dextran with 15 ml concentrated HCl and 250 ml MeOH and reactingthe product with hydrazine and $NaNO_2$ to give dextran azide which (100 mg) was stirred with 10 mg com. I in 5 ml H_2O 16 hr at 4° to give pellets containing I covalently linked to the carrier. The stability was measured by incubating in a mixture of 9 parts by volume phosphate buffer and 1 part by volume **human** blood at pH 7 and 37°. The polymer-supported I remained stable for 17 days while a com. I preparation showed a decrease of activity in 3 days. Other suitable polymers are cellulose, proteins, and synthetic polymers. I may be linked via diisocyanates, BrCN, Woodward reagent (N-ethyl-5-phenylisoxazolium-3'-sulfonate), or anhydride groups, e.g. maleic anhydride copolymers.

L7 ANSWER 67 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1970:421527 Document No. 73:21527 Spectrophotometric method for the determination of the kinetic characteristics of L-**asparaginase**. Mistretta, A. P.; Tassi, G. C.; De Barbieri, Augusto (Lab. Biochim., Ist. Sieroter. Milanese, Milan, Italy). Bollettino - Societa Italiana di Biologia Sperimentale, 45(16), 1120-3 (Italian) 1969. CODEN: BSIBAC. ISSN: 0037-8771.

AB L-**Asparaginase** from guinea pig serum showed no loss of activity after storage for 3 weeks in frozen state; the enzyme was also stable at temps. above 50°. Maximal activity was obtained at 65°, and activation energy was 8.2-8.4 kcal/mole. The activity was inhibited completely by p-chloromercuribenzoate (10-2M) and slightly by cysteine-HCl, ascorbic acid, iodoacetamide, and EDTA. No activity was found in serum from **humans**, horses, rabbits, and mice.

L7 ANSWER 71 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1970:99044 Document No. 72:99044 L-**Asparaginase** and inhibition of the lymphocyte immune reaction. Burgio, G. R.; Astaldi, A., Jr.; Krc, I.; Micu, D.; Astaldi, G. (Pediat. Clin., Univ. Med. Sch. Pavia, Pavia, Italy). Farmaco, Edizione Scientifica, 25(2), 85-95 (English) 1970. CODEN: FRPSAX. ISSN: 0430-0920.

AB The effect of Escherichia coli L-**asparaginase** (I) (0.10 IU/ml) on the blastogenesis of **human** peripheral blood lymphocytes was studied in vitro and in vivo. I markedly inhibited the blastogenic transforming process of the lymphocytes in cell culture, occurring either when the lymphocytes were stimulated with phytohemagglutinin (0.01-.16 mg/ml) or pokeweed mitogen, as well as in the mixed lymphocyte cultures. I (1 IU/ml) was effective in causing maximal blastogenesis inhibition, similar results being obtained with 5-10 IU; however 0.5 IU/ml caused 50% inhibition, whereas 0.1 IU/ml had no effect. I was completely inhibitory for blastogenesis, not only when added at the very beginning of the culture, but also when added anytime within 1 hr after initiation of the culture, suggesting that the enzyme inhibited blastogenesis not only via a cell surface mechanism, but also via a cellular metabolic mechanism. When I (200-800 IU/kg) was administered i.v. in vivo, the removed lymphocytes did not undergo phytohemagglutinin blastogenesis in cell culture added to their own serum. Lymphocytes, however, from enzyme-treated subjects underwent blastogenesis to the normal extent when cultivated with serum from patients not treated with the enzyme. Serum from patients i.v. injected with the enzyme inhibited the blastogenesis of lymphocytes from nonenzyme-treated patients. The addition of the I phytohemagglutinin culture to glutamic (1-5 mg/ml), asparagine (0.5-1 mg/ml), or aspartic acid (0.2 mg/ml) partially improved the lymphocyte blastogenesis. I may cause a complex imbalance in the amino acid composition of the plasma, rather than a selective depletion of 1 single amino acid.

L7 ANSWER 72 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1970:65290 Document No. 72:65290 **Human** blood level profile after administration of two different L-**asparaginases**. Puetter, Johann; Gehrmann, G. (Inst. Exp. Pathol., Farbenfabriken Bayer A.-G., Wuppertal-Elberfeld, Fed. Rep. Ger.). Klinische Wochenschrift, 47(24), 1324-6 (German) 1969. CODEN: KLWOAZ. ISSN: 0023-2173.

AB Twenty patients with malignant diseases were administered L- **asparaginase** A from Escherichia coli or L-**asparaginase** X, a chemical modified form of L-**asparaginase** A. The mean half-life elimination time from plasma was 11 hr after application of L- **asparaginase** A and 24 hr after application of L-**asparaginase** X. The blood levels of L-**asparaginase** X increased during daily injections until the 7th day, whereas no increase of blood L-**asparaginase** A was observed after ≤10 daily injections.

L7 ANSWER 79 OF 93 CAPLUS COPYRIGHT 2004 ACS on STN
1968:493065 Document No. 69:93065 L-**Asparaginase**: the evolution of a new tumor inhibitory agent. Broome, J. D. (Sch. of Med., New York Univ., New York, NY, USA). Transactions of the New York Academy of Sciences, 30(5), 690-704 (English) 1968. CODEN: TNYAAE. ISSN: 0028-7113.

AB Early work leading to the identification of L-**asparaginase** (I) as the tumor inhibiting agent in guinea pig serum is reviewed together with the effects on tumors of I from other sources. The types of tumors, particularly those in **humans**, known to be sensitive to I are described and evidence is presented indicating that lymphomas sensitive to I have a lower capacity to synthesize asparagine than resistant lymphomas and lack an asparagine synthetase. 40 references.